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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,628	09/05/2006	Hirohiko Hohjoh	U 016154-7	2748

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LADAS & PARRY LLP
26 WEST 61ST STREET
NEW YORK, NY 10023

EXAMINER

CHONG, KIMBERLY

ART UNIT	PAPER NUMBER
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1635

NOTIFICATION DATE	DELIVERY MODE
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09/03/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

nyuspatactions@ladas.com

Office Action Summary	Application No. 10/568,628	Applicant(s) HOHJOH, HIROHIKO	
	Examiner KIMBERLY CHONG	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 May 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 24, 25, 27 and 28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-23 and 26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>05/13/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 05/13/2009 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 11/13/2008 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed 05/13/2009, claims 1-28 are pending, claims 24-25 and 27-28 are withdrawn and claims 1-23 and 26 are currently under examination.

Information Disclosure Statement

The submission of the Information Disclosure Statement on 05/13/2009 is in compliance with 37 CFR 19.7. The information disclosure statement has been considered by the examiner and signed copies have been placed in the file.

Claim Rejections - 35 USC § 102 - maintained

The rejection of claims 1-23 and 26 under 35 U.S.C. 102(e) as being anticipated by Zamore et al. (US 2005/0186586 cited on PTO Form 892 mailed 01/24/2008) as evidenced by Aravin et al. (Developmental Cell, 2003 cited on PTO Form 892 mailed

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01/24/2008) and Elbashir et al. (Nature 2001 cited on PTO Form 892 mailed 01/24/2008) is maintained for the reasons of record.

Applicant's arguments filed 05/13/2009 have been fully considered but they are not persuasive. Applicant argues the dsRNAs disclosed by Zamore et al. in Figure 6 are miRNA sequences and not siRNA and miRNA control the translation of a gene differently than siRNA in that it causes gene silencing with no degradation of the target mRNA. Applicant further argues that dsRNAs disclosed by Zamore et al. are deduced to be generated by Dicer cleavage of naturally occurring miRNA precursors therefore the mismatches found between sense and antisense strands of the dsRNAs are generated naturally and not artificially introduced or designed such as instantly claimed.

These arguments are not convincing. The dsRNAs taught by Zamore et al. meet all of the structural requirements of the instant claims and therefore would be capable of suppressing the expression of a target gene in a cell by RNAi, absent evidence to the contrary. See MPEP 2112.01, "Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the *prima facie* case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product.

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In re Best, 562 F.2d at 1255, 195 USPQ at 433.” See also MPEP 2112: “[T]he PTO can require an Applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [her] claimed product.” The MPEP at 2112 citing *In re Fitzgerald* 205 USPQ 594. 596, (CCPA 1980), quoting In re Best 195 USPQ 430 as per above.

Zamore et al. teach in paragraph 0287 that the structures in Figure 6 are siRNA structures that were designed to mimic the structures of miRNA after cleavage by Dicer and these molecules meet all the limitations of the instant claims. Applicant's arguments that the mismatches found between the sense and antisense strand were not designed is not persuasive. Because the dsRNA structures taught by Zamore et al. meet all of the limitations of the instant claims and are in fact synthesized to be identical to naturally occurring miRNA sequences i.e. designed, these dsRNA would be capable of suppressing expression of a target gene in a cell by RNAi, absent evidence to the contrary.

Thus, Zamore et al. anticipates the instant claims.

Claim Rejections - 35 USC § 103 - maintained

The rejection of claims 1-23 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jayasena et al. (US 20040248299), Khvorova et al. (US 2007/0031844), Elbashir et al. (EMBO Journal 2001, Vol. 20, No. 23: 6877-6888) and Holen et al. (Nucleic Acids Research 2002, Vol. 30, No. 8: 1757-1766) is maintained for the reasons of record.

Applicant's arguments filed 05/13/2009 have been fully considered but they are not persuasive. Applicant argues that it was well known in the art that single stranded RNA is more susceptible to degradation by RNase than double stranded RNA and if the structure had mismatches on the end the siRNA would be expected to be easily degraded and those skilled in the art would never try to incorporate mismatches into siRNA molecules. Applicant argues the mismatches disclosed by Elbashir et al. and Holen et al. are between the antisense strand of siRNA and the target mRNA and not between the antisense strand and the sense strand.

Applicant's arguments are not convincing. It was clearly recognized by Jayasena et al. and Khvorova et al. that mismatches at the ends of the duplex allowed for the antisense guide strand to more efficiently load into RISC and therefore the skilled artisan would incorporate mismatches into siRNA molecules to increase the efficiency of the guide strand entering RISC thereby increasing the efficiency of RNAi. Furthermore it was well known in the art, and taught by Jayasena et al., Khvorova et al. and Elbashir et al., that incorporation of chemical modifications of dsRNA molecules protected the molecule against degradation by nucleases and the skilled artisan would be capable of designing stable dsRNA while improving the efficiency of RNAi by incorporation of mismatches at the ends of the duplex. Furthermore, one of ordinary skill in the art would have recognized from Holen et al. the desirability to investigate the tolerance of the RNAi system for mismatches in the siRNA relative to the mRNA target.

In regard to Applicant's argument that the mismatches taught by Elbashir et al. and Holen et al. are between the antisense strand and the target mRNA, this argument

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is not convincing. The sense strand of a dsRNA used to inhibit the expression of a mRNA is designed to contain the exact sequence of the target mRNA (see the cited references), therefore the antisense strand with a mismatch to the target would in fact also have a mismatch to the sense strand. Figure 6 of Holen et al. clearly exemplify a dsRNA with one or two mismatches relative to the sense strand which also be mismatches relative to the target sequence.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Thursday between 6 and 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Kimberly Chong/
Primary Examiner
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